Patient

Name:
Date of Birth:
Sex: Male
Case Number: TN22-
Diagnosis: Urothelial carcinoma, NOS

Specimen Information

Primary Tumor Site: Bladder neck
Specimen Site: Bladder, NOS
Specimen ID:
Specimen Collected:
Test Report Date:

Ordered By

Results with Therapy Associations

BIOMARKER	METHOD	ANALYTE	RESULT	THERAPY ASSOCIATION	BIOMARKER LEVEL*
PD-L1 (22c3)	**IHC**	**Protein**	**Positive, CPS: 10**	**BENEFIT** **pembrolizumab**	**Level 1**
BRCA1	Seq	DNA-Tumor	Pathogenic Variant Exon 19 | c.5277+1G>C	carboplatin, cisplatin olaparib A pathogenic or likely pathogenic BRCA1 mutation, and/or deletion, was detected in the tumor for which germline status is negative or unavailable for interpretation of therapy associations. The strongest evidence for DNA-damaging agents like PARP inhibitors or platinum compounds comes from studies that included predominantly germline mutations. Additionally, prescribing information and consensus guidelines (e.g. NCCN) for PARP inhibitors state a requirement for germline mutations. Therefore, the clinical benefit of these therapies in the context of tumor/somatic-only mutations (including deletions) remains to be fully determined.	

* Biomarker reporting classification: Level 1 – Companion diagnostic (CDx); Level 2 – Strong evidence of clinical significance or is endorsed by standard clinical guidelines; Level 3 – Potential clinical significance. Bolded benefit therapies, if present, highlight the most clinically significant findings.

Important Note

Invasive high-grade urothelial carcinoma with focal squamous and sarcomatoid differentiation was noted(**XXXX-XXXXX**)in this tumor. The squamous differentiation was evident in RNA expression in MI GPSai algorithm and matches the tumor to squamous cell carcinoma. Clinical correlation is warranted. A pathogenic mutation that disrupts an intron splice site was detected in BRCA1 Confirmation of the patient's carrier status should be considered.

This PD-L1 CPS is sufficient for use of pembrolizumab in the front-line metastatic setting. Use of pembrolizumab is FDA approved for the treatment of locally advanced or metastatic bladder cancer who are not eligible for cisplatin-containing chemotherapy with a PD-L1 CPS≥10, or in patients who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status. CPS is calculated as the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total viable tumor cells, multiplied by 100.

Cancer-Type Relevant Biomarkers

Biomarker	Method	Analyte	Result
ATM	**CNA-Seq**	**DNA-Tumor**	**Deleted**
	Seq	DNA-Tumor	Mutation Not Detected

Biomarker	Method	Analyte	Result
MSI	Seq	DNA-Tumor	Stable

(continued on next page)

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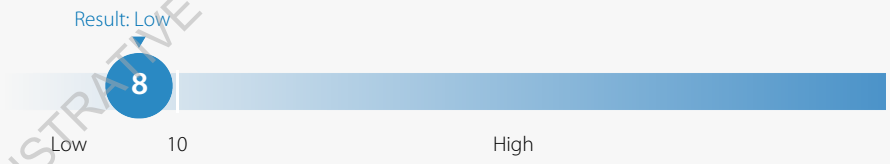
Cancer-Type Relevant Biomarkers (continued)

Biomarker	Method	Analyte	Result
Mismatch Repair Status	IHC	Protein	Proficient
NTRK1/2/3	Seq	RNA-Tumor	Fusion Not Detected
Tumor Mutational Burden	Seq	DNA-Tumor	Low, 8 mut/Mb
ERBB2 (Her2/Neu)	Seq	DNA-Tumor	Mutation Not Detected
ERCC2	CNA-Seq	DNA-Tumor	Deletion Not Detected
	Seq	DNA-Tumor	Mutation Not Detected
FANCC	CNA-Seq	DNA-Tumor	Deletion Not Detected
	Seq	DNA-Tumor	Mutation Not Detected
FGFR1	Seq	RNA-Tumor	Fusion Not Detected
FGFR2	Seq	RNA-Tumor	Fusion Not Detected
		DNA-Tumor	Mutation Not Detected
FGFR3	Seq	RNA-Tumor	Fusion Not Detected
		DNA-Tumor	Mutation Not Detected
MTAP	CNA-Seq	DNA-Tumor	Indeterminate
PD-L1 (SP142)	IHC	Protein	Negative, IC: 0%
TSC1	CNA-Seq	DNA-Tumor	Deletion Not Detected
	Seq	DNA-Tumor	Mutation Not Detected

Genomic Signatures

Biomarker	Method	Analyte	Result
Microsatellite Instability (MSI)	Seq	DNA-Tumor	Stable
Tumor Mutational Burden (TMB)	Seq	DNA-Tumor	
Genomic Loss of Heterozygosity (LOH)	Seq	DNA-Tumor	Low - 6% of tested genomic segments exhibited LOH (assay threshold is ≥ 16%)

Genes Tested with Pathogenic or Likely Pathogenic Alterations

Gene	Method	Analyte	Variant Interpretation	Protein Alteration	Exon	DNA Alteration	Variant Frequency %
ATM	CNA-Seq	DNA-Tumor	Deleted	-	-	-	-
BRCA1	Seq	DNA-Tumor	Pathogenic Variant	c.5277+1G>C	19	c.5277+1G>C	23
FBXW7	Seq	DNA-Tumor	Pathogenic Variant	p.Q242*	4	c.724C>T	78
KMT2D	Seq	DNA-Tumor	Pathogenic Variant	p.L3152fs	34	c.9455 _9461del7	25
	Seq	DNA-Tumor	Pathogenic Variant	p.P648fs	10	c.1940dupC	51
SDHD	CNA-Seq	DNA-Tumor	Deleted	-	-	-	-

Additional results continued on the next page. >

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Genes Tested with Pathogenic or Likely Pathogenic Alterations

Gene	Method	Analyte	Variant Interpretation	Protein Alteration	Exon	DNA Alteration	Variant Frequency %
TP53	Seq	DNA-Tumor	Pathogenic Variant	p.R282fs	8	c.845 _849delGGCGC	83

Unclassified alterations for DNA sequencing can be found in the MI Portal.
Formal nucleotide nomenclature and gene reference sequences can be found in the Appendix of this report.
Variants of Uncertain Significance can be found in the MI Portal.

Human Leukocyte Antigen (HLA) Genotype Results

The impact of HLA genotypes on drug response and prognosis is an active area of research. These results can help direct patients to clinical trials recruiting for specific genotypes. Please see www.clinicaltrials.gov for more information.

Gene	Method	Analyte	Genotype
MHC CLASS I			
HLA-A	Seq	DNA-Tumor	A*29:02, A*68:01
HLA-B	Seq	DNA-Tumor	B*14:02, B*35:01
HLA-C	Seq	DNA-Tumor	C*04:01, C*08:02

HLA genotypes with only one allele are either homozygous or have loss-of-heterozygosity at that position.

Immunohistochemistry Results

Biomarker	Result	Biomarker	Result
MLH1	Positive | 2+, 70%	PD-L1 (22c3)	Positive, CPS: 10
MSH2	Positive | 2+, 80%	PD-L1 (SP142)	Negative, IC: 0%
MSH6	Positive | 2+, 80%	PMS2	Positive | 2+, 80%

Genes Tested with Indeterminate Results by Tumor DNA Sequencing

COL2A1	MGA	NFE2L2	NPM1	PIK3CB	PIK3R2	PLCB4	PTPRD	RASA1	SOS1	STAG2	XRCC2
MED12											

Genes in this table were ruled indeterminate due to low coverage for some or all exons.

Genes Tested with Intermediate CNA Results by Tumor DNA Sequencing

APOBEC3B	ERBB2 (Her2/Neu)	FGF3									

PATIENT: **TN22-** **PHYSICIAN:**

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